



PATENT
Our Docket: 066654-604 (P-LJ 4575)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:) Examiner: M. Yu
Ruoslahti et al.)
Serial No.: 09/765,086) Group Art Unit: 1642
Filed: January 17, 2001) Confirmation No.: 6131
For: CHIMERIC PROSTATE-HOMING)
PEPTIDES WITH PRO-APOPTOTIC)
ACTIVITY)

Commissioner For Patents
Post Office Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION UNDER 37 C.F.R. § 1.131

We, Erkki I. Ruoslahti, Renata Pasqualini, Wadih Arap, Dale E. Bredesen and H. Michael Ellerby, declare as follows:

1. We, Erkki I. Ruoslahti, Renata Pasqualini, Wadih Arap, Dale E. Bredesen and H. Michael Ellerby, are named as co-inventors of the above-identified application.
2. We understand that the claimed invention stands rejected, in part, as allegedly obvious in view of Ellerby et al., "Anti-cancer activity of targeted pro-apoptotic peptides," Nature Medicine 5: 1032-1038 (1999), which was published in September of 1999.
3. This Declaration attests that we made the claimed invention prior to publication of the above Ellerby et al. publication. Documentary evidence in support thereof is attached hereto as Exhibits 1 and 2.

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4. Prior to September of 1999, we conducted research directed to the ability of a chimeric peptide containing a prostate-homing peptide linked to an antimicrobial peptide to cause selective cell death in prostate following intravenous administration.
5. As evidence that we had conceived and obtained a chimeric prostate-homing pro-apoptotic peptide containing the prostate-homing sequence "SMSIARL" and the antimicrobial sequence "(KLAKLAK)₂," attached is a photocopy of a CaP CURE Research Award proposal submitted by Dr. Wadih Arap, who was a Senior Research Associate in Dr. Erkki Ruoslahti's laboratory at the time. The dates on the CaP CURE Research Award Proposal have been redacted but are prior to September of 1999.
6. Specifically, Exhibit 1 attached hereto is a copy of the CaP CURE Research Award Proposal with a facsimile cover sheet indicating that a copy of the proposal was faxed to the Burnham Institute by an individual at the CaP CURE organization.
7. The abstract on the "Face Sheet" of the proposal indicates that a prostate-homing peptide was used to deliver a pro-apoptotic peptide to prostate blood vessels and that, following intravenous administration, the prostate-targeted compound induced massive cell death selectively in the prostate. Figures 2 and 3 (page 2) show that peptide SMSIARL homes specifically to the prostate. Page 3, first full paragraph, indicates that the antimicrobial peptide (KLAKLAK)₂ was chosen as a prototype to be targeted by a prostate-homing peptide to prostate blood vessels.

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8. As described at page 3, second full paragraph, and shown in Figure 5, the prostate-targeted compound SMSIARLKLAKLAKKLAKLAK was administered to male mice and resulted in specific cell death in the prostate but not in other organs. These results demonstrate that a chimeric peptide containing the prostate-homing peptide SMSIARL and the antimicrobial peptide (KLAKLAK)₂ was prepared and shown to selectively induce cell death in prostate tissue *in vivo*.
9. The results discussed in paragraphs 6 to 8 above show that we had obtained a chimeric prostate-homing pro-apoptotic peptide containing a prostate-homing peptide linked to an antimicrobial peptide prior to September of 1999. The results discussed in paragraphs 6 to 8 above further show that, prior to September of 1999, we had demonstrated selective cell death in prostate tissue *in vivo* following administration of a chimeric peptide containing a prostate-homing peptide linked to an antimicrobial peptide.
10. As additional corroboration of the dates on which the CaP CURE Research Award Proposal was complete, attached as Exhibit 2 is electronic correspondence from Angelica Diega at CaP CURE. Although the dates on the correspondence have been redacted, the correspondence indicates that the research proposal was received by CaP CURE, and an award check sent prior to September of 1999.
11. I do not know and do not believe that the invention was in the public prior to the time I conceived of the invention and reduced it to practice and I have never abandoned the application.

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I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that willful false statements may jeopardize the validity of the application or any patent issuing thereon.

2-9-04

Date



Erkki I. Ruoslahti

Date

Renata Pasqualini

Date

Wadih Arap

Date

Dale E. Bredesen

Date

H. Michael Ellerby

R E C E I V E D
MAR 12 2004

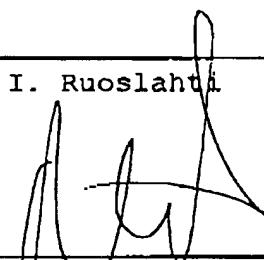
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McDERMOTT, WILL & EMERY

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Date

Erkki I. Ruoslahti



Date

Renata Pasqualini



Date

March 12, 2004

Wadih Arap

Date

Dale E. Bredesen

Date

H. Michael Ellerby

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Erkki I. Ruoslahti

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Renata Pasqualini

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Date
Dale E. Bredesen

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Date

Erkki I. Ruoslahti

Date

Renata Pasqualini

Date

Wadih Arap

Date

Dale E. Bredesen

Date

3/4/04

H. Michael Ellerby

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